

WHAT IS CLAIMED IS:

1. A method for identifying a compound active on a biologically active STAAU_R9 polypeptide comprising the amino acid sequence of SEQ ID NO: 6, or a biologically active variant thereof, wherein said polypeptide specifically binds to a bacteriophage polypeptide sequence, said method comprising:

contacting said STAAU_R9 polypeptide with a candidate compound, and

detecting one of: a binding of said compound to said STAAU_R9 polypeptide; and a biological activity thereof, wherein said binding of the compound to said STAAU_R9 polypeptide or a decrease in said biological activity thereof in the presence of said candidate compound relative to same in the absence thereof, is indicative that said candidate compound is a compound that is active on the STAAU_R9 polypeptide.

2. The method of claim 1, wherein said STAAU_R9 polypeptide is contacted simultaneously with said bacteriophage polypeptide sequence.

3. The method of claim 1 or 2, wherein said binding or said decrease in biological activity is performed in the presence and absence of said candidate compound.

4. The method of one of claims 1 to 3, wherein said bacteriophage polypeptide sequence is selected from the group consisting of:

- a) SEQ ID NO:4; and
- b) a fragment or variant of a) that specifically binds with SEQ ID NO:6.

5. The method of one of claims 1 to 4, wherein said detecting comprises measuring the binding of a candidate compound to said STAAU_R9 polypeptide, wherein the compound is directly or indirectly detectably labeled.

5 6. A method for identifying a compound active on one of a STAAU_R9 polypeptide and a bacteriophage polypeptide which specifically interacts with same comprising:

contacting said STAAU_R9 polypeptide which comprises the amino acid sequence of SEQ ID NO: 6, or variant thereof, and said bacteriophage polypeptide which is selected from the group consisting of:

10 a) SEQ ID NO:4; and
b) a fragment or variant of a), wherein said fragment or variant of a) maintains its biological activity;
with a candidate compound; and

15 detecting a biological activity of said STAAU_R9 polypeptide and/or said bacteriophage polypeptide, wherein a decrease in the biological activity thereof in the presence of the candidate compound is indicative that said candidate compound is a compound that is active on one of said STAAU_R9 and/or bacteriophage polypeptide.

20 7. The method of claim 6, which identifies a compound active on STAAU_R9.

25 8. The method of claim 6 or 7, wherein said detecting comprises the act of measuring the binding of said STAAU_R9 polypeptide to said bacteriophage polypeptide wherein said STAAU_R9 polypeptide or said bacteriophage polypeptide is directly or indirectly detectably labeled.

30 9. A method of identifying a compound that is active on a biologically active STAAU_R9 polypeptide, said method comprising:

10. An agonist or an antagonist of the activity of a STAAU_R9 polypeptide or fragment thereof, or a nucleic acid encoding said polypeptide or fragment thereof, identified with any one of the methods of claims 1 to 9.

12. The method of any one of claims 1-8, wherein said detecting comprises measurement of fluorescence polarization changes.

14. The method of any one of claims 1-8, wherein said detecting comprises a scintillation proximity assay.

16. The method of any one of claims 1-8, wherein said
30 detecting comprises measurement by phage display.

17. A method of making an antibacterial compound, comprising:

- 5 identifying a compound active on a polypeptide comprising the amino acid sequence selected from:
- a) SEQ ID NO:2;
 - b) a biologically active fragment or variant of a) capable of binding specifically to a bacteriophage polypeptide sequence;
 - c) SEQ ID NO:6; and
 - 10 d) a biologically active variant of c) or fragment thereof capable of binding specifically to a bacteriophage polypeptide sequence; and
 - e) a nucleic acid encoding any of said polypeptide of a) – d), wherein said polypeptide is capable of binding specifically to a bacteriophage polypeptide sequence; and
- 15 synthesizing or purifying said active compound in an amount sufficient to provide a therapeutic effect when administered to an organism infected by a bacterium naturally producing said polypeptide, or nucleic acid encoding same.

- 20 18. A method for inhibiting a bacterium, comprising contacting the bacterium with a compound active on one of a) a *S. aureus* polypeptide comprising the amino acid sequence of SEQ ID NO: 2, fragment or variant thereof; b) a *S. aureus* polypeptide comprising the amino acid sequence of SEQ ID NO: 6, fragment or variant thereof; and c) a nucleic acid encoding the
- 25 polypeptide of a) or b), wherein said fragment or variant retains its biological activity in binding to a bacteriophage ORF.

19. A method for treating or preventing a bacterial infection in an animal suffering from an infection or at risk of suffering therefrom, comprising
- 30 administering to said animal a therapeutically effective or prophylactic effective

amount of a compound active on a *S. aureus* polypeptide comprising the amino acid sequence of one of a) SEQ ID NO: 2, fragment or variant thereof; b) SEQ ID NO: 6 fragment or variant thereof; c) a nucleic acid encoding said amino acid sequence of a) or b), wherein said fragment or variant retains its biological activity in binding to a bacteriophage ORF.

20. A method of prophylactic treatment to prevent bacterial infection comprising contacting an indwelling device with a compound active on a *S. aureus* polypeptide comprising the amino acid sequence of SEQ ID NO: 6, capable of binding to a bacteriophage ORF, before its implantation into a mammal, such contacting being sufficient to prevent *S. aureus* infection at the site of implantation.

21. A method of prophylactic treatment to prevent infection of an animal by a bacterium comprising administering to the animal a compound that is active on a *S. aureus* polypeptide comprising one of the amino acid sequence of SEQ ID NO: 2, fragment or variant thereof; SEQ ID NO: 6, fragment or variant thereof; or a gene encoding said polypeptide, wherein same is capable of specifically interacting with a bacteriophage polypeptide, in an amount sufficient to reduce adhesion of the bacterium to a tissue surface of a tissue of the mammal.

22. The method of any one of claims 1-9, or 11-21, wherein said active compound is selected from the group consisting of a small molecule, a peptidomimetic compound, and a fragment or derivative of a bacteriophage inhibitor protein.

23. The method of any one of claims 1-9, or 11-21, wherein said active compound is a peptide synthesized by an expression system and purified, or is artificially synthesized.

24. The method of claim 23, wherein said compound is selected from the group consisting of:

- 5 a) SEQ ID NO:4; and
 b) a fragment or variant of a), wherein said fragment or variant thereof maintains its specific binding capability of interacting with one of SEQ ID NO:2, SEQ ID NO: 6, fragment or variant thereof.

10 25. The method of any one of claims 18, 20, 22, 23 or 24, wherein said contacting is performed *in vitro*.

 26. The method of any one of claims 18, 19, 21-23 or 24, wherein said contacting is performed *in vivo* in an animal.

15 27. The method of any one of claims 18-26, wherein said contacting is performed in combination with existing antimicrobial agents.

20 28. The method of any one of claims 1-9, 10, 11-16, or 22-24, wherein said STAAU_R9 polypeptide comprises the amino acid sequence as set forth in SEQ ID NO:2, or biologically active fragment or variant thereof.

25 29. A composition comprising an isolated, purified or enriched bacteriophage 96 ORF 78-encoded polypeptide; and a *S. aureus* STAAU_R9 polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 6, fragment or variant thereof, which retains its biological activity in binding to said bacteriophage ORF.

30 30. A composition comprising a pair of specifically interacting domains, said pair comprising: a STAAU_R9 polypeptide and a polypeptide encoded by a bacteriophage ORF which specifically interacts with said

STAAU_R9 polypeptide, wherein at least one of said interacting domains is isolated, purified or enriched.

5 31. The composition of claim 30, wherein said STAAU_R9 polypeptide comprises the amino acid sequence set forth in SEQ ID NO:6, and wherein said bacteriophage ORF comprises the amino acid sequence as set forth in SEQ ID NO:4.

10 32. The composition of claim 30 or 31, wherein said STAAU_R9 polypeptide comprises the amino acid sequence set forth in SEQ ID NO:2 or biologically active fragment or variant thereof.

15 33. A process for producing a pharmaceutical composition comprising: a) identifying a compound that is active on a STAAU_R9 polypeptide by performing a screening assay for compounds active on a polypeptide comprising the amino acid sequence of SEQ ID NO:6, or biologically active fragment or variant thereof, that binds specifically with a second polypeptide derived from a bacteriophage ORF; and b) mixing the compound identified in a) with a suitable pharmaceutical carrier.

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34. The process of claim 33, wherein said bacteriophage ORF comprises the amino acid sequence as set forth in SEQ ID NO:4.

25 35. The process of claim 33 or 34, wherein said STAAU_R9 polypeptide comprises the amino acid sequence as set forth in SEQ ID NO:2 or biologically active fragment or variant thereof.

30 36. Use of one of: a) a STAAU_R9 polypeptide comprising the amino acid sequence of SEQ ID NO:2, a biologically active fragment or variant thereof; wherein said STAAU_R9 polypeptide is capable of binding specifically to

a polypeptide derived from a bacteriophage ORF;b) a STAAU_R9 polypeptide comprising the amino acid sequence of SEQ ID NO:6, a biologically active fragment or variant thereof, wherein said STAAU_R9 polypeptide is capable of binding specifically to a polypeptide derived from a bacteriophage ORF, c) a composition comprising a pair of specifically interacting domains comprised of a polypeptide of STAAU_R9, biologically active fragment thereof or variant thereof and a polypeptide encoded by a bacteriophage ORF which specifically interacts with STAAU_R9; or d) an assay mixture comprising a first polypeptide which comprises one of i) the amino acid sequence of SEQ ID NO:2, ii) the amino acid sequence of SEQ ID NO:6, or iii) a biologically active fragment or variant of i) or ii); and a second polypeptide encoded by a bacteriophage ORF which specifically interacts with one of i)-iii); for the identification of a compound that is active on a STAAU_R9 polypeptide.

37. The method of any one of claims 17-19, 21, 24 or 28, wherein said biologically active fragment or variant of SEQ ID NO:2 comprises an amino acid sequence of SEQ ID NO:2 mutagenized in the portion which is absent in SEQ ID NO:6.

38. The composition of claim 32, wherein said biologically active fragment or variant of SEQ ID NO:2 comprises an amino acid sequence of SEQ ID NO:2 mutagenized in the portion which is absent in SEQ ID NO:6.

39. The process of claim 35, wherein said biologically active fragment or variant of SEQ ID NO:2 comprises an amino acid sequence of SEQ ID NO:2 mutagenized in the portion which is absent in SEQ ID NO:6.

40. An isolated polypeptide comprising the amino acid sequence as set forth in one of:

a) 1-599 of SEQ ID NO:2;

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- b) 35-599 of SEQ ID NO:2;
- c) 229-599 of SEQ ID NO:2;
- d) 380-599 of SEQ ID NO:2;
- e) 449-599 of SEQ ID NO:2;
- f) 490-599 of SEQ ID NO:2;
- g) 530-599 of SEQ ID NO:2;
- h) 561-599 of SEQ ID NO:2; and
- i) a biologically active variant of a) to h);

to screen and identify antibacterial compounds.

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41. The isolated polypeptide of claim 40, wherein said amino acid sequence is as set forth in SEQ ID NO:6.

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42. An isolated polypeptide consisting of the amino acid sequence as set forth in one of:

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- a) 1-599 of SEQ ID NO:2;
- b) 35-599 of SEQ ID NO:2;
- c) 229-599 of SEQ ID NO:2;
- d) 380-599 of SEQ ID NO:2;
- e) 449-599 of SEQ ID NO:2;
- f) 490-599 of SEQ ID NO:2;
- g) 530-599 of SEQ ID NO:2;
- h) 561-599 of SEQ ID NO:2; and
- i) a biologically active variant of a) to h);

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to screen and identify antibacterial compounds.

43. The isolated polypeptide of claim 42, wherein said amino acid sequence is as set forth in SEQ ID NO:6.

44. An isolated nucleic acid sequence encoding the amino acid sequence of claim 40, 41, 42 or 43.

5 45. An isolated, purified or enriched antibody specific for an isolated polypeptide of claim 40, 41, 42, 43 or 44.

46. The antibody of claim 45, specific for a polypeptide of SEQ ID NO:6.

10 47. The method of claim 23, wherein said expression system is cell-based.